Defining unit operations for integrated, dynamic single-cell analyses

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The majority of analytical technologies used to assess the identities and functional capacities of cells yield average measures of their phenotypes. These measures obscure unique individuals that contribute significantly to the collective behavior or that may be of particular interest in discovery-based research. This talk will describe the development of a collection of techniques that use microfabricated arrays of subnanoliter containers (10^5-10^6) that define modular unit operations for integrating biological measurements across multiple scales and time. Two specific applications of these technologies for massively parallel single-cell analyses will be presented. First, an integrated analysis of individual cells within a clonal population of Pichia pastoris—a yeast used for production of heterologous proteins in biomanufacturing—reveals new insights to the dynamics of secretion by individual clones and how non-genetic variations alter the uniformity of the population. The implications of these factors on the challenges of strain engineering for biomanufacturing will be discussed. Second, the talk will outline how similar approaches to assessing lineages and functions can start to improve the resolution of clinical monitoring in human diseases, particularly for chronic human diseases such as HIV/AIDS. The approaches described provide a new basis for advanced clinical monitoring of cellular responses to candidate vaccines and highly quantitative diagnostics.

Professor Love is an assistant professor in chemical engineering at MIT. He is also an Associate Member at the Eli and Edythe L. Broad Institute, and Associate Faculty at the Ragon Institute of MGH, MIT, and Harvard. Professor Love graduated with a B.S. degree in chemistry from the University of Virginia in 1999 (conducted research with Cassandra Fraser). He received his Ph.D. in 2004 in physical chemistry at Harvard University under the supervision of George Whitesides. Following completion of his doctoral studies, he extended his research into immunology with Hidde Ploegh at Harvard Medical School from 2004-2005, and at the Immune Disease Institute from 2005-2007. His current research uses microsystems to characterize heterogeneity among single cells with specific studies in HIV/AIDS, autoimmunity, and biopharmaceutical manufacturing. He was named a Dana Scholar for Human Immunology and a Keck Distinguished Young Scholar in Medical Research in 2009.